

What is claimed is:

1. A crystalline venlafaxine base wherein the venlafaxine base is in the form of white crystals.
2. A crystalline venlafaxine base according to claim 1, wherein the venlafaxine base has a purity of greater than about 99.3%.
3. A process for preparing a crystalline venlafaxine base having a purity of greater than about 99.3% and in the form of white crystals comprising the step of adding sodium hydroxide to an aqueous solution of venlafaxine hydrochloride.
4. A process according to claim 3, further comprises extracting the aqueous solution with an organic solvent to form an organic solution.
5. A process according to claim 4 wherein the organic solvent is selected from the group consisting of ethyl acetate, heptane, hexane and a mixture thereof.
6. A process according to claim 5, further comprises drying the organic solution over anhydrous sodium sulfate.
7. A process according to claim 6, further comprises filtering the organic solution to remove residues.
8. A process according to claim 7, wherein the residues are dissolved in boiling hexane or heptane and cooled down.
9. A process according to claim 8, further comprises adding hydrochloric acid to venlafaxine base and crystallizing venlafaxine hydrochloride.
10. A crystalline venlafaxine hydrochloride having a purity of greater than about 99.3% produced according to claim 9.
11. A process for preparing a crystalline venlafaxine base having a purity of greater than about 99.3% and in the form of white crystals comprising the step of adding sodium hydroxide to an aqueous solution of N,N-didesmethyl venlafaxine hydrochloride.
12. A process according to claim 11, further comprises adding a formic acid and a formaldehyde solution.

13. A process according to claim 12, further comprises extracting the aqueous solution with an organic solvent to form an organic solution.
14. A process according to claim 13, wherein the organic solvent is solvent is selected from the group consisting of ethyl acetate, heptane, hexane and a mixture thereof.
15. A process according to claim 13, wherein the organic solvent is heptane.
16. A process according to claim 14, further comprises drying the organic solution over anhydrous sodium sulfate.
17. A process according to claim 16, further comprises filtering the organic solution to remove residues.
18. Venlafaxine hydrochloride Form I', characterized by powder x-ray diffraction peaks at 10.2, 15.5, 20.3, 21.7 ± 0.2 degrees two-theta.
19. Venlafaxine hydrochloride Form I, characterized by powder x-ray diffraction peaks at degrees two-theta 6.7, 10.2, 13.5, 15.5, 18.2, 19.8, 20.3, 21.7, 22.6, 25.6, 28.1, 35.1 ± 0.2 degrees two-theta.
20. Venlafaxine hydrochloride Form II, characterized by powder x-ray diffraction peaks at 12.8, 20.5, 21.3 ± 0.2 degrees two-theta.
21. Venlafaxine hydrochloride Form II, characterized by powder x-ray diffraction peaks at 6.8, 8.5, 10.3, 12.8, 13.6, 15.6, 16.5, 19.1, 19.9, 20.5, 21.3, 21.9, 25.2, 28.7, 31.2, 31.7, 35.3 ± 0.2 degrees two-theta.
22. Venlafaxine hydrochloride Form III characterized by powder x-ray diffraction peaks at 7.4, 14.9, 26.5 ± 0.2 degrees two-theta.
23. Venlafaxine hydrochloride Form III characterized by powder x-ray diffraction peaks at 7.4, 12.9, 14.9, 16.4, 17.5, 18.6, 18.9, 20.5, 21.4, $26.5, 38.2 \pm 0.2$ degrees two-theta.
24. Venlafaxine hydrochloride solvate characterized by powder x-ray diffraction peaks at 7.4, 14.9, 26.5 ± 0.2 degrees two-theta.
25. Venlafaxine hydrochloride solvate characterized by powder x-ray diffraction peaks at 7.4, 12.9, 14.9, 16.4, 17.5, 18.6, 18.9, 20.5, 21.4, $26.5, 38.2 \pm 0.2$ degrees two-theta.

26. Venlafaxine hydrochloride of any one of claims 24 through 25, wherein the solvate is selected from the group consisting of ethanolate, methanolate and isopropanolate.
27. Venlafaxine hydrochloride Form IV characterized by powder x-ray diffraction peaks at 10.3, 13.5, 15.6, 20.3 ± 0.2 degrees two-theta.
28. Venlafaxine hydrochloride Form IV characterized by powder x-ray diffraction peaks at 6.8, 10.3, 13.5, 15.6, 20.3, 21.8, 27.2, 35.2 ± 0.2 degrees two-theta.
29. Venlafaxine hydrochloride solvate characterized by powder x-ray diffraction peaks at 10.3, 13.5, 15.6, 20.3 ± 0.2 degrees two-theta.
30. Venlafaxine hydrochloride solvate characterized by powder x-ray diffraction peaks at 6.8, 10.3, 13.5, 15.6, 20.3, 21.8, 27.2, 35.2 ± 0.2 degrees two-theta.
31. Venlafaxine hydrochloride of any one of claims 29 through 30, wherein the solvate contains a solvent selected from the group consisting of DMSO and DMF.
32. A process for preparation of products of any one of claims 22 through 25, the process comprises dissolving venlafaxine hydrochloride in a protic solvent and crystallizing it by the addition of an aprotic solvent.
33. A process according to claim 32, wherein the protic solvent is selected from the group consisting of water, methanol and ethanol.
34. A process according to claim 32, wherein the aprotic solvent is selected from the group consisting of acetone, ethyl acetate, isopropyl ether, and MTBE.
35. A process for preparation of products of any one of claims 22 through 25, the process comprises crystallizing venlafaxine hydrochloride in a protic solvent.
36. A process according to claim 35, wherein the protic solvent is selected from the group consisting of ethanol and isopropanol.

37. A process for preparation of product of any of claims 27 through 30, the process comprises crystallizing venlafaxine hydrochloride in an aprotic polar solvent.
- 5 38. A process according to claim 37, wherein the aprotic polar solvent is selected from the group consisting of DMF and DMSO.
39. A process for preparation of venlafaxine hydrochloride Form I comprises dissolving venlafaxine hydrochloride in water and crystallizing it by the addition of an aprotic solvent.
- 10 40. A process according to claim 39, wherein the aprotic solvent is selected from the group consisting of MEK and DMF.
41. A process for preparation of venlafaxine hydrochloride Form II comprises dissolving venlafaxine hydrochloride in a mixture of a protic solvent and an aprotic solvent.
42. A process according to claim 41, wherein the protic solvent is methanol.
- 15 43. A process according to claim 41, wherein the aprotic solvent is ethyl acetate.
44. A process according to claim 41, wherein the ratio of the solvent: antisolvent: venlafaxine hydrochloride is 10ml: 30ml: 3 grams.
- 20 45. A process where the product in any one of claims 22 through 25 is dried to obtain venlafaxine hydrochloride Form I, venlafaxine hydrochloride Form II or a mixture thereof.
46. A process where the product of any one of claims 27 through 30 is dried to obtain venlafaxine hydrochloride Form III, venlafaxine hydrochloride Form IV, or a mixture of thereof.
- 25 47. A process for preparation of the product of any one of claims 22 through 25, the process comprises dissolving venlafaxine hydrochloride in chloroform and crystallizing it by the addition of any of hexane and toluene.

48. A process for preparation of products of any one of claims 22 through 25, the process comprises triturating venlafaxine hydrochloride in an aprotic solvent under a reflux condition for at least 1 hour.
49. A process for preparation of products of any one of claims 22 through 25, the process comprises triturating venlafaxine hydrochloride in an aprotic solvent at room temperature for at least a period of about 20 hours.
50. A process for preparing venlafaxine hydrochloride, comprising the steps of:
- 1) preparing a mixture of venlafaxine in acetone; and
 - 2) exposing the mixture in gaseous hydrochloric acid.
51. A process according to claim 50, wherein venlafaxine is a venlafaxine base.
52. A process according to claim 50, wherein the mixture is a homogeneous solution of venlafaxine.
53. Venlafaxine hydrochloride prepared by a process of claim 50.
54. Venlafaxine hydrochloride as in claim 53, wherein the venlafaxine hydrochloride is a white crystal with about 99.92% purity.
55. A process for preparing venlafaxine hydrochloride Form I comprises triturating venlafaxine hydrochloride with acetone followed by drying upon stirring under reduced pressure.
56. Venlafaxine hydrochloride Form I as prepared by a process of claim 55.
57. Venlafaxine hydrochloride Form I as in claim 56, wherein the venlafaxine hydrochloride Form I is a white crystal with about 99.95% purity.
58. A process for preparing venlafaxine hydrochloride Form II comprises triturating venlafaxine hydrochloride with acetone followed by drying in a tray under reduced pressure.
59. Venlafaxine hydrochloride Form II as prepared by a process of claim 58. Venlafaxine hydrochloride Form II as in claim 58, wherein the

venlafaxine hydrochloride Form II is a white crystal with about 99.95% purity.

60. A crystalline venlafaxine hydrochloride solvate, wherein the venlafaxine hydrochloride solvate contains a solvent.
- 5 61. A crystalline venlafaxine hydrochloride solvate according to claim 60, wherein the venlafaxine hydrochloride solvate crystal form is Form III.
62. A crystalline venlafaxine hydrochloride solvate according to claim 60, wherein the venlafaxine hydrochloride solvate crystal form is Form IV.
63. A crystalline venlafaxine hydrochloride solvate Form III according to
10 claim 61, wherein the solvent is selected from the group consisting of water, ethanol, methanol and isopropanol.
64. A crystalline venlafaxine hydrochloride solvate Form III according to claim 61, wherein the solvate crystal form contains about 5.6% to about 6.0% methanol solvent.
- 15 65. A crystalline venlafaxine hydrochloride solvate Form III according to claim 61, wherein the solvate crystal form contains about 5.6% to about 6.0% ethanol solvent.
66. A crystalline venlafaxine hydrochloride solvate Form III according to
20 claim 61, wherein the solvate crystal form contains about 4.6% isopropyl alcohol.
67. A crystalline venlafaxine hydrochloride solvate Form III according to claim 61, wherein the solvate crystal form contains about 5.5% hexane solvent.
68. A crystalline venlafaxine hydrochloride solvate Form IV according to
25 claim 62, wherein the solvent is selected from the group consisting of DMSO and DMF.
69. A crystalline venlafaxine hydrochloride solvate Form IV according to claim 68, wherein the solvate crystal form contains about 41% DMSO solvent.

70. A crystalline venlafaxine hydrochloride solvate Form IV according to claim 68, wherein the solvate crystal form contains about 33% DMF solvent.
- 5 71. A crystalline venlafaxine hydrochloride solvate Form III, wherein the Form III contains a solvent selected from the group consisting of methanol and ethanol.
72. A crystalline venlafaxine hydrochloride solvate Form III according to claim 71, wherein the amount of solvent is in a stoichiometric ratio of $\frac{1}{2}$ molecule of solvent per molecule of venlafaxine hydrochloride.
- 10 73. A crystalline venlafaxine hydrochloride solvate Form III, wherein the Form III contains an isopropyl alcohol solvent and the amount of solvent is in a stoichiometric ratio of $\frac{1}{4}$ molecule of solvent per molecule of venlafaxine hydrochloride.
- 15 74. A crystalline venlafaxine hydrochloride solvate Form IV, wherein the Form IV contains a DMSO solvent and the amount of solvent is in a stoichiometric ratio of 3 molecules of solvent per molecule of venlafaxine hydrochloride.
- 20 75. A crystalline venlafaxine hydrochloride solvate Form IV, wherein the Form IV contains a DMF solvent and the amount of solvent is in a stoichiometric ratio of 2 molecules of solvent per molecule of venlafaxine hydrochloride.